

**Notice of Allowability**

Application No.

10/695,140

Examiner

William W. Moore

Applicant(s)

KUKOLJ ET AL.

Art Unit

1656

-- **The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to the amendment filed 10 August 2006 and the interview conducted 13 September 2006.
2. ☒ The allowed claim(s) is/are 18, 19, and 21-24.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) ☐ All    b) ☐ Some\*    c) ☐ None    of the:
  1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
  5. ☐ CORRECTED DRAWINGS ( as "replacement sheets") must be submitted.
    - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review ( PTO-948) attached
      - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
    - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

- |   |  |
|---|--|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892)  | 5. <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)            |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                | 6. <input type="checkbox"/> Interview Summary (PTO-413),<br>Paper No./Mail Date _____. |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO-1449 or PTO/SB/08),<br>Paper No./Mail Date _____ | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment                    |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit<br>of Biological Material          | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance   |
|   | 9. <input type="checkbox"/> Other _____.   |

## EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Cancel claims 12-17 and 20.

Amend claims 18-24 thus:

18. (Amended) A method for identifying ~~a potential a second generation~~ inhibitor of HCV

NS3 protease activity comprising:

incubating an inhibitor-resistant NS3 protease variant ~~mutant~~ as defined in

claim 19 ~~4~~ in the presence or absence of a candidate ~~second generation~~

inhibitor compound; and

measuring the protease activity of said inhibitor-resistant NS3 protease in the

presence and absence of said candidate ~~second generation~~ inhibitor

compound;

wherein a decrease in activity of said protease in the presence of a candidate

~~second generation~~ inhibitor indicates that said compound inhibits said ~~inhibitor-~~

~~resistant~~ HCV NS3 protease.

19. (Amended) An isolated, A variant, inhibitor-resistant, HCV NS3 protease having serine protease activity comprising an HCV NS3 protease amino acid sequence wherein said variant comprises a substitution of ~~numbered according SEQ ID NO:2~~ wherein the amino acid at the position corresponding to at position 156 of SEQ ID NO:2 ~~is substituted~~ with a non-alanine amino acid.

21. (Amended) The variant protease according to claim 19 ~~4~~, wherein said amino acid sequence set forth in ~~comprises~~ SEQ ID NO:2, ~~and further~~ comprises an amino acid

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~~at least one~~ substitution selected from the group consisting of: A156G<sub>±</sub>, A156T<sub>±</sub>, and A156V.

22. (Amended) The variant protease according to claims 19 or 21 ~~4 or 2~~, further comprising one or more amino acid substitutions selected from the group consisting of S20N, R26K, Q28R, A39T, Q41R, I71V, Q80R, Q86R, P89L, P89S, S101N, A111S, P115S, S122R, R155Q, L144F, A150V, R155W, V158L, D168A, D168G, D168H, D168N, D168V, E176K, T178S, M179I, M179V, and M179T ~~a P89S~~ substitution.
23. (Amended) An isolated, A variant, inhibitor-resistant, HCV NS3 protease comprising an amino acid sequence which is at least 90% identical to the amino acid sequence of SEQ ID NO:2, wherein said variant comprises an amino acid comprising at least one substitution at the position corresponding to position 156 of SEQ ID NO:2 selected from the group consisting of: A156G<sub>±</sub>, A156T<sub>±</sub>, and A156V.
24. (Amended) The variant protease according to claim 23 ~~5~~, further comprising one or more amino acid substitutions selected from the group consisting of S20N, R26K, Q28R, A39T, Q41R, I71V, Q80R, Q86R, P89L, P89S, S101N, A111S, P115S, S122R, R155Q, L144F, A150V, R155W, V158L, D168A, D168G, D168H, D168N, D168V, E176K, T178S, M179I, M179V, and M179T ~~a P89S substitution~~.

Authorization for this examiner's amendment was given in a telephone interview with Mr. David Dow on 13 September 2006.

The following is an examiner's statement of reasons for allowance:

The examiner's amendment cancels claim 20 which became a substantial duplicate of claim 19 upon the entry of Applicant's amendments filed 10 August 2006, rejoins and amends claim 18 in view of the above amendment permitting the allowance of claims 19 and 21-24, provides the term "inhibitor-resistant" in claim 19 so that claim 18 may

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properly depend from claim 19, and replaces the term "mutant" in claim 18 with the term "variant" found in claim 19. The examiner's amendment also removes the unnecessary phrase "at least one" in claims 21 and 23 because each of the substitutions identified in these claims occur at the same amino acid position, thus no multiple substitutions may occur at that position, and replaces the term "numbered according to" with a phrase requiring that the invention be practiced with a "HCV NS3 protease amino acid sequence" that "comprises an amino acid substitution at the position corresponding to position 156 of SEQ ID NO:2" according to the description provided at page 13, lines 19-21, of the specification. In view of the numerous native HCV NS3 protease amino acid sequences sharing at least 75% sequence identity with SEQ ID NO:2 listed in the PIR 79 database sequence search results of 15 September 2005 entered for this application in the USPTO's SCORE database, one of ordinary skill in the art can readily determine which is the position in any native HCV NS3 protease amino acid sequence that corresponds to the highly-conserved alanine at position 156 of SEQ ID NO:2 herein as well as positions corresponding to those recited for the further amino acid substitutions of claims 22 and 24 as amended above. Finally, since the product claims 19, 21 and 23 recite substitutions that are free of the prior art of record, the several species of other substitutions recited in the original claims 6-8 are joined together with the elected species of substitution, P89S, in claims 22 and 24 amended above.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

#### *Conclusion*

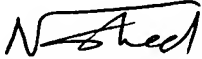
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For

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more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Dr. Kathleen Kerr, can be reached at 571.272.0931. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

William W. Moore  
13 September 2006

  
NASHAAT T. NASHED PHD.  
PRIMARY EXAMINER